sistent area of marked epigastric sensitiveness the size of an egg to the left of the median line, to the outer side of the left rectus. Its relation to the area of greatest muscular rigidity was not noted. Operation advised. It was three hours later before he could decide on his course, be gotten to the hospital and prepared for operation. Grumous material and inflammatory exudate covered the gastric and colonic surfaces beneath the area of special tenderness, but it was not specially restricted to that locality. Recent adhesions were present between stomach and abdominal wall. All parts exposed showed an intensely inflamed peritoneum; that portion beneath the seat of marked sensitiveness not as pronounced as that more adjacent to the location of the ulcer. **The perforation was found, not at the left beneath the most tender area, but on the opposite side** close to the pylorus near the lesser curvature. Recovery ensued.

Case 4. C., male, age 51 years, was first seen nine hours after perforation. He had been originally taken to a hospital in a neighboring city, where diagnosis was not made, but a hypodermic of morphine administered. Neither water nor whisky swallowed after onset caused gastric distress. His previous history as to ulcer was not convincing. He was without fever and in good general condition. He did not seem seriously ill, nor was he apparently must distressed. His abdomen was only moderately contracted. **The left side was decidedly the more rigid.** There was only a mild, **diffuse,** epigastric tenderness. There was, however, an area of marked sensitiveness, sharply localized beneath the **left rectus about 5 cm. below the level of the umbilicus,** beneath the most rigid portion of the abdominal parietes. Colonic irrigation was without result. The water returned with an apparent slight bloody tinge with sanguino-mucous flakes. Diagnosis was in doubt. The aggregate of symptoms and physical findings seemed to indicate a lower intestinal, rather than a gastric or duodenal lesion. Operation three hours later. Incision was made in the midline below the umbilicus. Everywhere was present the evidence of pronounced, diffuse, septic peritonitis. Beneath the area of special tenderness, there was a small, rather localized collection of sero-purulent and flaky exudate. The cecal and left transverse colonic regions, where special symptoms of irritation were not noticeable before operation, showed, however, the same condition. This incision was closed except at its lowermost portion where a pelvic drain was placed. The epigastrium was then opened and **perforation was found distant from and on the side opposite to the site of greatest sensitiveness,** close to the pylorous, at the lesser curvature. Recovery ensued.

Can these findings be reconciled with the generally recognized symptomatology and with the numerous apparently contradictory operative observations? The following is offered as a possible solution:

The portion of peritoneum at the site of perforation, in certain instances, being subjected to continuous, prolonged irritation from an unusually concentrated and irritating extruded gastric contents, to which the tissues of some individuals may react differently than those of others, may after a time, lose something of its sensitiveness and fail to respond to increased stimulation by palpation. This condition would only be analagous to the well recognized depression of nerve function, even paralysis, resulting from overstimulation in other parts of the body of motor, and special sense nerves. Or as a result of local toxic and inflammatory influences, actual changes may take place in the delicate peritoneal nerve terminals that prevent the conduction of pain impulses.[3] Coincidentally, other areas coming within the zone of spreading irritation, either for some reason naturally more sensitive or having been subjected to a less overpowering degree of irritation, by reason of their distance from the ulcer, may at this later period and at least temporarily, be relatively more keenly alive to pressure than is the original focus from which the irritation has come. That the greatest abdominal wall protective rigidity should then be over these now more sensitive parts does not seem to be strange or unreasonable; or that, as these new peritoneal areas are involved, symptoms referable to the newly affected part may stand out, at least for a time, with conspicuous boldness and attract and unduly hold the surgeon's attention.

At times the approximate site of perforation is susceptible of fairly close determination. But again, with an incomplete antecedent and recent history, a knowledge of which the sufferings of the patient or the ignorance or nervousness of his associates prevent the surgeon from gaining; with an atypical symptomatology; with other symptoms resulting from almost necessary complications of the primary disease pressing to the front and obscuring the original state; with the usual signs of morbidity dissipated or altered by injudicious narcotic medication, the clinical picture may be so changed, that the diagnostic skill of the well informed surgeon may be overtaxed.

This much, at least, is demanded in the presence of general peritonitis: If the local tenderness and other signs seem to indicate that the appendix is involved, before its surgical approach, the duodenum should be questioned and first given clearance. If localized tenderness exists in other abdominal areas, no matter how low down, the stomach and duodenum, both, should be considered as possible original sources of trouble, and passed upon. After the lapse of several hours from the time of perforation, local abdominal tenderness must be cautiously judged and discriminatingly received, if at all, as a directing symptom. The possible falsifying peritoneal tendency as to localized tenderness demands its accurate collation with all other symptoms of the condition in question together with a consideration of the stage of the disease and the available history.

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## THE BUTYRIC ACID TEST OF NOGUCHI AS AN AID IN DIAGNOSIS.*

By F. F. GUNDRUM, M. D., Sacramento.

The cerebro-spinal fluid is the liquid which bathes the brain and spinal cord, acting, first, as a hydraulic cushion to protect against jars; second, as a medium to carry away waste products; and third,

3. Prof. Maxwell, of the Department of Physiology, University of California, informs the writer that the possibility of paralysis from overstimulation is positively determined in sensory nerves. As to the conduction of pain impulses, the matter has not, so far as he is aware, been actually worked out; he regards it, however, not improbable. He advanced the suggestion of the possible depression of the function of pain conduction from toxic effects on the nerve terminals, as a probable added factor in this special condition.

* Read before the California Northern District Medical Society, at Sacramento, California, November 11, 1913.

as a reservoir to regulate intracranial pressure. The whole amount of the spinal fluid, at any one time, is uncertain, possibly in an adult from 50 to 90 CC. The fluid is actively secreted from the choroid plexuses in the lateral ventricles. The tangled web of blood vessels in these organs is covered by a single layer of flattened cells which have their origin in the posterior wall of the embryonic neural canal, and are, therefore, epiblastic in origin. The spinal fluid is secreted by them into the cavities of the lateral ventricles. It flows from the two lateral ventricles through the foramina of Monroe, into the third ventricle, thence through the aqueduct of Sylvius into the fourth ventricle. From here the larger portion passes through minute openings in the roof of the fourth ventricle, the foramina of Magendie, and spreads out over the cortex of the cerebrum and downwards in the subdural spaces of the cord, where it is taken up by the lymphatics and veins of the dura and returned to the general circulation. A smaller portion penetrates the central canal of the cord. The fluid under normal conditions is a water-clear, alkaline liquid under a pressure of approximately 100 mm. of water. It does not coagulate when left to stand; the specific gravity varies between 1002 and 1010.

It is considered abnormal to find more than about eight white blood cells to each c. mm. of fluid; usually there are but one or two; these belong to the group of lymphocytes. Chemically, the fluid shows but a faint trace (.03 to .06%) of proteid and a small amount (0.1%) of dextrose, enough to give a slight reduction of Fehling's solution.

Under the influence of diseases of the central nervous system, the spinal fluid undergoes certain alterations in physical, cellular and chemical characteristics.

1. The physical properties may become changed in the following ways: a. Cloudy fluids. These cloudy fluids generally indicate an extravasation of white blood cells into the cerebro-spinal fluid—in other words, a meningitis. Microscopical examination usually easily determines what type of invading organism is the cause of the turbidity observed. b. Bloody fluids. These are seen particularly after fractures of the bony canal protecting the spine or skull, and are often an early evidence of fracture at the base.

2. Changes may take place in the cellular contents. a. Polymorphonuclear cells may be greatly increased as is commonly seen in the cerebro-spinal meningitis, influenzal meningitis, etc. b. Lymphocytes may show marked increase in numbers as in tuberculous meningitis and lues. c. Increase in red cells often follows injury done by the needle upon entry. This blood is small in amount and a few seconds of flow clears the needle. The presence of blood from such a slight injury differs very greatly from the abundant crimson flow often seen after cranial fracture.

3. Marked changes may also take place in the chemical reaction of the fluid. The capacity for reducing Fehling's solution may be lost. The proteid content may or may not be increased. It is upon this latter chemical characteristic (the presence or absence of a demonstrable increase in proteid content) that this series of 43 cases was recorded. There are several common tests for the determination of the excess of albumen.

1. Nonne's. The fluid is mixed with an equal quantity of warm saturated ammonium sulphate solution. The appearance of turbidity or precipitate declares a positive test.

2. The hydrochloric acid test of Braun & Husler. Only 1 cc. of cerebro-spinal fluid is required for this test. To this is added 1 cc. at a time, a solution of .003 normal hydrochloric acid. If after 5 cc. are added, no precipitate forms, the reaction is negative. It is desirable that a freshly prepared solution of the acid be used.

3. The butyric acid test devised by Noguchi. Two parts of cerebro-spinal fluid are mixed with five parts of 10% butyric acid in normal salt solution and the mixture is brought to a brief boiling. Then one part of normal sodium hydroxide solution is added and the fluid brought to a second brief boiling. The appearance within fifteen minutes of a flocculent or granular whitish precipitate constitutes a positive test. A faint turbidity without flocculi is to be considered negative.

During the past three years at the Sacramento County Hospital we have obtained for study the cerebro-spinal fluid of 43 cases in which pathological, microscopical or other laborator examinations made the clinical diagnosis undoubted. Thus we had data at hand for the estimation of the ultimate value of the butyric acid test in clinical diagnosis. These cases easily fell into two groups.

1. Those in which cloudy fluids were obtained. Of these, ten were spinal meningitis and two secondary meningitis due to pneumococcus. These, of course, were all positive as would be expected. The fluids were centrifuged and the clear portions only used for the tests. In 31 instances clear fluids were obtained. The list of diseases included here is a varied one. It embraces a heterogeneous group of maladies in which some symptoms referable to damage in the cerebro-spinal axis developed. Positive reactions were obtained in tabes, general paresis, tuberculous meningitis, poliomyelitis and rabies. Negative reactions were obtained in endocarditis, old poliomyelitis, old hemiplegia, bronchopneumonia, cerebellar tumor, typhoid, sunstroke, uremia, delirium tremens, influenza and lobar pneumonia. The group of negatives seems to include very many remotely allied maladies, but in all of them, at the time the lumbar puncture was made, there was some symptom or sign suggesting a possible involvement of the brain, cord or meninges. The accompanying chart represents more graphically the diagnosis made clinically and those made later pathologically, with the result of the butyric acid test in the right-hand column.

## BUTYRIC ACID TEST.

### (A.)—Cloudy. Fluids.

Fluids centrifuged and clear portions used for test.

| | Diagnosis. Clinical. | Pathological. | Butyric Acid test. |
|---|---|---|---|
| 1 | Cerebro-spinal meningitis | Diplococcus | Posit. |
| 2 | " " " | Diplococcus of Weischelbaum | Posit. |
| 3 | " " " | " " | Posit. |
| 4 | " " " | | |
| 5 | " " " | " " | Posit. |
| 6 | " " " | " " | Posit. |
| 7 | " " " | " " | Posit. |
| 8 | " " " | " " | Posit. |
| 9 | " " " | " " | Posit. |
| 10 | " " " | " " | Posit. |
| 11 | Secondary meningitis | Pneumococcus | Posit. |
| 12 | " " | " | Posit. |

### (B.)—Clear. Fluids.

| | | | |
|---|---|---|---|
| 1 | Cerebral lues | Wassermann (Noguchi) | Posit. |
| 2 | Tuberculous meningitis | Autopsy tubercles | Posit. |
| 3 | Acute rheumatism Endocarditis meningismus | | Negat. |
| 4 | Poliomyelitis (old) | | Negat. |
| 5 | Lues spinal | Wassermann (Noguchi) | Posit. |
| 6 | Lues spinal | Gummata in skin | Posit. |
| 7 | Hemiplegia (old) | | Negat. |
| 8 | Pulmonary tuberculosis | Cavities in lungs | Negat. |
| 9 | Tuberculous meningitis | Broncho-pneumonia | Negat. |
| 10. | Uremia (?) | Tuberculous meninges | Posit. |
| 11 | Multiple sclerosis | | Negat. |
| 12 | Cerebro-spinal lues | Wassermann (Noguchi) | Posit. |
| 13 | Tabes dorsalis (classical) | | Posit. |
| 14 | Cerebellar tumor | Glioma (autopsy) | Negat. |
| 15 | Lues | Wassermann (Noguchi) | Posit. |
| 16 | Poliomyelitis (acute) | Flaccid paralysis | Posit. |
| 17 | Tuberculous meningitis | Tubercles on pia | Posit. |
| 18 | Tuberculous meningitis | Tubercles on meninges | Posit. |
| 19 | Meningitis (typhoid) | Typhoid fever (meningismus) | Negat. |
| 20 | Tuberculous meningitis | Tubercular bacilli (guinea pig) | Posit. |
| 21 | Cerebro-spinal lues | Wassermann (Noguchi) | Posit. |
| 22 | Cerebellar tumor | Glioma (autopsy) | Negat. |
| 23 | Tuberculous meningitis | Tubercles in meninges | Posit. |
| 24 | Tabes dorsalis | clinically typical | Posit. |
| 25 | Sunstroke | | Negat. |
| 26 | Uremia | Chronic nephritis | Negat. |
| 27 | General paresis | Clinically typical | Posit. |
| 28 | Rabies | Inoculation tests positive | Posit. |
| 29 | Cerebro-spinal lues | Wassermann (Noguchi) | Posit. |
| 30 | Delirium tremens | | Negat. |
| 31 | Influenza | B. Influenza in sputum | Negat. |
| 32 | Pneumonia lobar (meningismus) | Autopsy | Negat. |

The butyric acid test was not controlled by any of the other tests for albumen increase in this series, but merely by the autopsy and pathological findings in each case. Cases were reported in which ultimate diagnosis beyond reasonable doubt, was made through autopsy, miscroscopical or other laboratory method.

### CONCLUSIONS.

1. In this small series of 43 cases, the butyric acid test was positive in all instances where marked inflammation or degeneration was going on in the cerebro-spinal system.

2. It was absent in diseases where, although there seemed to be spinal involvement, no actual organic nervous lesion was present.

3. In all doubtful cases simulating inflammatory diseases of the brain or spinal cord, spinal puncture is indicated. If the fluid is turbid, the butyric acid test is superfluous. If the fluid is clear, the butyric acid test enables us to tell whether or not inflammatory or degenerative changes are taking place.

4. In other diseases where symptoms of meningeal irritation arise, the obtaining of a clear spinal fluid which fails to show the butyric acid test of Noguchi, is of considerable moment, particularly in the matter of prognosis.

#### References.

1. Noguchi. Serum Diagnosis of Syphilis, 3rd edition. Lippincott, pp. 221-239.
2. Batteis and Lederer. J. A. M. A., Vol. LX, No. 2, p. 811, March 15, 1913.
3. Strouse. J. A. M. A., Vol. LVI, No. 16, p. 1171, April 22, 1911.
4. Karpas. J. A. M. A., Vol. LXI, No. 4, p. 262, July 26, 1913.